

Appln. No.: 10/672,225
Amendment Dated March 8, 2007
Reply to Office Action of December 8, 2006

RCHP-125US1

Amendments to the Drawings:

The attached sheet of drawings includes changes to Figure 1. This sheet replaces the original sheet.

Attachment

Remarks/Arguments:

Claims 1-30 are pending in the application. Claims 23-30 are withdrawn as directed to an unelected invention. The office action states that claim 19 is also withdrawn as part of unelected Group II, but Applicants submit that this is in error because claim 19 recites a dithio group as the reactive moiety on the surface, and the dithio group is a thiol-reactive group as elected under 3(b). See page 8 at line 31.

Information Disclosure Statement

Applicants are submitting concurrently herewith legible copies of the non-patent literature publications disclosed in the Information Disclosure Statement filed April 22, 2004, as requested by the Office Action.

In addition, Applicants respectfully request confirmation of the Patent Office's consideration and initialing of the following references cited in the Information Disclosure Statement dated January 20, 2004:

U.S. 5,674,298

10/672,893 (now issued as U.S. 6,890,998).

The initialed copies of Applicants' IDS forms do not currently reflect consideration of these references.

Drawings

Fig. 1 is objected to under 37 CFR 1.83(a) because Fig. 1 fails to show "thiol-reactive dithio groups of product 3" as described in the specification, e.g., page 9, line 7, or "thiol groups of product 3" as described in the specification, e.g., page 10, lines 12-13. Applicants thank the examiner for bringing these deficiencies to their attention. Applicants' review of the Figures and the specification indicates that Fig. 1 does indeed show what was intended, and properly supports a correct understanding of the invention, but reveals that some elements in Figs. 1 and 2 were referred to in the text by incorrect numbers.

Specifically, the passage at page 9, line 7 (and in fact all of the references to "product 3" in the section titled "Thiol-Containing Fluorophores") should have referred to "product 5", not product 3. Appropriate amendments to the specification are made herewith. Also, the second sentence of that section should have referred to Fig. 2, not Fig. 1. Thus, that sentence is amended herewith to read:

"Either of these groups can be reacted with a suitable reagent to furnish product 35 (as shown in FIG. 12) that comprises thiol-reactive groups. The preferred thiol-reactive group is a dithio group."

Support for these explanations may be found in Examples 2 and 6, where the proper identities of products 3 and 5 are described respectively, as well as by the fact that only by correction of these typographical errors does the specification make logical sense. Applicants submit that these amendments obviate the objection and the need for corrected drawings, and request that the objection now be withdrawn.

Similarly, the passage at page 10, lines 12-13 (and in fact all of the references to "product 3" in the section titled "Thiol-Reactive Fluorophores") should have referred to "product 4", not product 3. Appropriate amendments to correct this typographical error are submitted herewith.

During the course of reviewing Fig. 1, Applicants discovered minor errors unrelated to the drawing objection set forth in the Office Action. In particular, Fig. 1 is amended herewith to show the proper number of carbon atoms in the butyl substituents, as supported on page 6 at lines 4-8 and in Example 1, as well as in the reagents shown in original Fig. 1.

No new matter has been added by any of the foregoing amendments.

35 U.S.C. § 112

Claims 1-3, 5-7, 12-14, 16, 20 and 22 are rejected under 35 U.S.C. § 112, 2nd paragraph, as indefinite.

In claims 1 and 2, the terms "adapted," "to form," "to liberate," and "to determine" have been deemed indefinite. The claims have been amended to overcome these rejections. Support for the new term "thereby liberating the fluorescent moiety from the surface" can be found on page 6 lines 16-18, which describes liberating the fluorescent material dansyl-L-cysteine into solution (i.e., liberating it from the surface).

In claim 2, the lack of antecedent basis for the term "the cleavable" has been corrected.

In claim 2, the recitation relating to a disulfide bond or an aromatic azo compound has been amended for clarity.

In claim 5, the recitation of "FI-SH" is deemed indefinite because the orientation of "-SH" with respect to fluorescent L-cysteine, BODIPY-L-cysteine, and fluorescein is not clear. The

claim has now been amended for clarity to recite that FI-SH is selected from the group consisting of L-cysteine derivatives bearing fluorescent substituents, and compounds wherein FI comprises a fluorescein moiety. The fluorescent moiety FI can be any fluorescent moiety, as indicated on page 6 at line 15, page 7 at line 12, and page 9 at lines 7-11. The orientation of SH is not critical to the invention, since its function is merely to tie the fluorescent moiety to the surface. However, Applicants note that numerous examples explicitly showing the orientation of -SH with respect to the fluorescent moiety are shown throughout the application. Thus, Applicants submit that this rejection has been overcome.

Claim 12 is further rejected under § 112 due to indefiniteness of the terms "is bound," "is reacted," "to form," and "predominantly." Claim 12 has been amended for clarity, rendering all of these bases for rejection moot, except for use of the term "is bound." The office action asserts that this term is indefinite, but cites no rule in support of this assertion. Applicants submit that the term "is bound" is clear, and that the identity of the objects required for binding are clear. Specifically, the binding is between the second reactive moiety and the fluorescent moiety, and is performed by a bond, namely a disulfide bond or an aromatic azo bond. Thus the rejection should be withdrawn.

Claims 1-2 are rejected as being incomplete for omitting essential steps. The claims have been amended to clarify that the binding capacity is calculated based on the strength of a signal from the liberated fluorescent moiety, and Applicants submit that the rejection has now been overcome. See page 13, lines 17-26 for support.

35 U.S.C. § 102

Claims 1-3, 5-7, 12-14, 16 and 20 have been rejected under 35 U.S.C. § 102(b) as anticipated by Pope et al., US 5,399,501 ("Pope"). The office action states that Pope discloses detecting a detectable signal, citing column 2 lines 18-19. The full paragraph from which the cited passage is abstracted states as follows:

"An alternative to centrifugation involves attaching at least one of the binding assay's reactants to a solid support. The solid support can then be separated from the test sample and the remaining assay reagents to provide for the separation of the free and bound label. The separation of the solid support and reaction mixture can be accomplished either by drawing-off the remaining reaction mixture or by physically removing the solid phase from the reaction mixture. The solid support can also be treated or washed to remove interfering substances prior to the detection or measurement of the label associated with the solid phase." [emphasis added]

As this passage states, only the label (which may be fluorescent) that is bound to the solid phase is measured according to Pope, who underscores this point by noting that interfering substances can be washed away first. Such washing would certainly remove any liberated fluorescent moiety (label), if any had been formed by cleaving a bond between that fluorescent moiety and the substrate as presently claimed. However, Pope does not cleave the label from the surface before analyzing for it, and thus Pope does not provide this claim element. Since rejection under § 102 requires that all of the claim elements be provided, the rejection has been overcome and should be withdrawn.

35 U.S.C. § 103

Claim 22 has been rejected under 35 U.S.C. § 103(a) over Pope in view of 56 J. Org. Chem. 2648 (1991) by Burns et al ("Burns"). As noted above, Pope does not disclose cleaving a fluorescent moiety from a surface and subsequently measuring a signal produced by it. The office action relies on Burns to provide the claim element of claim 22 relating to use of TCEP as the reducing agent, but Burns does not remedy the aforementioned deficiency of the Pope reference. Accordingly, not all claim elements have been provided by the combined references, and a *prima facie* case of obviousness has not been presented. Therefore, the rejection should be withdrawn.

Conclusion

Applicants submit that the application is now in condition for allowance, and respectfully request reconsideration and notification of same. Applicants invite the examiner to contact their undersigned representative, Frank Tise, if it appears that this may expedite examination.

Respectfully submitted,



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CAR/FPT/

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Attachments: Figure 1 (1 sheet)
Three non-patent literature publications

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Gayle D. Bay